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EXAMINER	
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ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/664,423	ROULEAU ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *14-22* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/10/03,5/16/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's remarks and amendments filed 1 June 2006 have been entered. Claims 14 – 22 are pending.

Election/Restrictions

2. Applicant's election with traverse of SEQ ID NO:1 in the reply filed on 1 June 2006 is acknowledged. The traversal is on the ground(s) that there would not be a serious burden to search all claimed sequences at once. This is not found persuasive because in contrast to applicant's assertion, there would in fact be a serious burden to search all sequences at once. For example, claim 14 encompasses four sequences, claim 15 encompasses thirty different sequences. Each sequence requires a separate search, and search for any one of these products will not determine if any other product is novel or non-obvious. Each sequence must be separately searched by the USPTO's computers, and given the length of the sequences, searching all sequences now claimed would present a serious burden on the available computer resources.

Applicant also argues that "all claimed sequences relate to the same gene" and therefore should be searched together. However, many of the sequences are of very different lengths and comprise different structural and functional regions. For instance, SEQ ID NO:1 is over 8000 nucleotides long, whereas SEQ ID NO:s 5 and 6 are 850 and 483 nucleotides, respectively. All these sequences, among others, are set forth in claim 15 and are also encompassed by independent claim 14. Searching SEQ ID NO:1 will not reveal whether the much shorter sequences are novel or non-obvious.

Applicant also points to MPEP § 803.04, suggesting that up to 10 independent nucleotide searches should be examined in a single application. Applicant is directed to the text immediately preceding the section he excerpted in his response, which states that

> "Polynucleotide molecules defined by their nucleic acid sequence (hereinafter "nucleotide sequences") that encode different proteins are structurally distinct chemical compounds. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq."

Applicant has not provided any evidence that the nucleic acids are not independent and distinct, and thus the presumption is that they are in fact independent and distinct. Furthermore, applicant did not point out which ten sequences should be examined of the thirty sequences set forth in claim 15. Applicant was explicitly invited to point out those structural elements common to all sequences to be searched and which are necessary for a common utility (see restriction requirement, p. 2, in the middle of the page) but declined to point out such structural features.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 14 – 22 are under examination.

Claim Objections

4. Claims 14 – 16 are objected to because of the following informalities: they recite non-elected subject matter. Claim 14 recites four sequences; the elected invention (SEQ ID NO:1) cannot possibly be in all four sequences. Claim 15 recites 30 sequences, but only one of them (SEQ ID NO:1) has been elected. Claim 16 recites two amino acid sequences, but the nucleic acid of SEQ ID NO:1 cannot encode them both. Appropriate correction is required.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 20 – 22 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are not limited to isolated host cells but rather encompass any cell harboring the requisite vectors. The specification appears to contemplate methods of gene therapy. For example, on p. 25, paragraphs 1 – 3, the inventors contemplate the use of the nucleic aicds in pharmaceutical compositions for treatment of disease. In light of the specification, the broadest reasonable interpretation of "a cell" as recited in claims 20 – 22 includes cells within a human being's body after the person has been treated in a gene therapy protocol. It appears applicant is attempting to claim human beings as his invention; human beings are not patentable.

Amendment to "An isolated host cell" is recommended to obviate this rejection

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 – 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid with the sequence of SEQ ID NO:1 and for isolated host cells comprising vectors which include the nucleic acid, does not reasonably provide enablement for all fragments, functional derivatives, or allelic variants as broadly set forth in claims 14 – 16. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

In this case, the nature of the invention, which is a nucleic acid that encodes a sodium channel and may be involved in the treatment of epilepsy, is complex. The nucleic acids set forth in claims 14 – 16 are not limited to SEQ ID NO:1, but are sufficiently broad to include any "fragment, functional derivative, or allelic variant thereof." The breadth of these terms includes essentially any fragment, of any size, or any variant. There is no requirement that any particular protein be encoded by the nucleic acid, or that the nucleic acid itself have any particular use, for example in gene therapy or the like. There is no requirement in the claims that the protein encoded by the claimed fragments, functional derivatives, or allelic variants have any particular amino acid sequence, or that the encoded protein have any particular function. Given that SEQ ID NO:1 has over 8000 nucleotides, the claims read on an essentially infinite number of possible fragments and functional derivatives. The specification discloses that SEQ ID NO:1 is the nucleic acid sequence of the adult form of SCN1A (see p. 27), which is a sodium channel. The specification also discloses that genomic DNA which encodes SCN1A is sometimes altered in

patients with certain forms of epilepsy (see for example p. 53). However, the specification does not teach the artisan how to use the fragments of the nucleic acid now claimed. While "fragments" are not explicitly defined in the specification, a very similar term "DNA segment" is in fact defined on p. 9. Clearly, as contemplated by the inventors, there is no upper or lower limit on the size of the segment or fragment. There is no use demonstrated or even contemplated for fragments as small as, for example, three nucleotides, and there is no requirement that any particular region be retained in the "fragment". Thus the skilled artisan would have to determine how to make the full scope of fragments of the nucleic acids, as well as how to use them. The claims do not require that the nucleic acid fragments, or the protein fragments encoded by them, have any particular activity or function. Given the lack of guidance in the specification commensurate with the scope of fragments, the artisan would have to determine how to use an unreasonably large number of members of this very broad genus on his or her own. Such a degree of experimentation, combined with the lack of guidance and dearth of working examples, would be undue.

Furthermore, the specification does not teach the artisan how to make a "functional derivative" as recited in claims 14 – 16. This term is defined explicitly in the specification at p. 17, final paragraph. The derivative, according to the definition, must be "substantially similar" in its activity, but there is no definition of how similar it must be, or what specific activities are to be retained by the functional derivative of the nucleic acid. In fact, one could alter a large percentage of the nucleotides in the claimed sequences, and they would still encode some protein with some function. However, there is no reason to believe that the encoded protein would be a sodium channel. As the specification only teaches the artisan how to use sodium channels, and not other proteins, it would be incumbent upon the artisan to discover how to use the "functional derivative[s]" as recited in claims 14 – 16. There is no reason to believe that the protein encoded by the "functional derivative" of SEQ ID NO:1 would be a sodium channel, or that it would have any biological function at all. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a [protein] sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Thus in order to determine how to use the functional derivatives as claimed, or the

proteins encoded by those functional derivatives, the artisan would have to resort to painstaking experimentation. Given the breadth of the claims and the lack of guidance commensurate with their very broad scope, the degree of experimentation required would be undue.

Similarly, the claims encompass any "allelic variant" of the disclosed nucleic acid. An allele is an alternative form of a gene, which varies from one person to another (see specification p. 19, first complete paragraph). The specification does disclose a few, very specific allelic variants of the SCN1A gene. For example, p. 52 of the specification discloses that some patients with idiopathic generalized epilepsy have a sequence which comprises SEQ ID NO:190, whereas the normal sequence of the nucleic acid comprises SEQ ID NO:189. Additionally, some patients with idiopathic generalized epilepsy have a sequence which comprises SEQ ID NO:191, whereas the normal sequence of the nucleic acid comprises SEQ ID NO:192. The claims, however, encompass any allelic variant, whether or not the variant results in a change in amino acid sequence. The variant may be present at any position in the nucleic acid sequence, and may be of any type (insertion, deletion, and substitution). The specification does not disclose a reasonable number of members of this very broad genus, and thus the burden would be on the artisan to discover the structures of the allelic variants. Furthermore, the artisan would have to discover how to use these allelic variants, once they had been invented. Given the breadth of the claims and the lack of disclosure of a reasonable number of allelic variants as broadly defined, the artisan would have to resort to an undue amount of experimentation in order to make and use the allelic variants commensurate in scope with the claims.

7. Claims 14 – 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims encompass not only the disclosed nucleic acid sequences, but also any "fragment, functional derivative, or allelic variant thereof" (see particularly claims 14 – 16), which are undefined by structure. The fragments, derivatives, and variants claimed have not been described in the specification. These variants are essentially without any structural or functional

limitation. The skilled artisan cannot envision the structures of the very broad genera of nucleic acids that are claimed because the specification does not describe them.

A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606." Here, applicant has not described the nucleic acids now claimed, but rather has mentioned that the variants, fragments, and derivatives are part of the invention and has sketched out a method of how the invention could be obtained. Thus claims 14 – 16 clearly fail to comply with the written description requirement. The remaining claims are rejected because they depend from rejected base or intermediate claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14 – 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Mandel (WO 96/14077, published 17 May 1996), as evidenced by Mandel (US Patent 6,110,672, issued 29 August 2000).

Mandel (WO 96/14077) teaches SEQ ID NO:14, which is a nucleic acid 6404 base pairs long. The attached sequence alignment shows the correspondence between applicant's SEQ ID NO:1 and SEQ ID NO:14 from Mandel (US 6,110,672). However as the '672 patent is the national-stage entry of the international application (see face page of the '672 patent), the disclosures are identical. Thus the alignment attached provides evidence that the Mandel WO 96/14077 reference, published more than a year before the earliest possible effective filing date of this application, anticipates the invention.

Mandel's SEQ ID NO:14 has 42.7% overall identity to applicant's SEQ ID NO:1. There are several large stretches of identity, including the regions from about base 479 – 502 and from about bases 1016 – 1041, using applicant's numbering system. These regions are fragments of SEQ ID NO:1. The scope of claims 14 – 16 includes nucleic acids which comprise fragments of SEQ ID NO:1. As Mandel's SEQ ID NO:14 comprises several fragments of SEQ ID NO:1, it anticipates the invention of claims 14 – 16.

On p. 13, Mandel WO 96/14077 teaches both vectors comprising the nucleic acids and host cells comprising same, thereby anticipating claims 17 – 19 and 20 – 22 respectively.

9. Claims 14 – 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Noda (1986. Nature 320:188 – 192), as evidenced by sequence alignment for NCBI Accession number X03638.

Noda teaches nucleic acid sequences encoding rat sodium channels. The nucleic acid sequences are depicted beginning on p. 189. The attached sequence alignment for between applicant's SEQ ID NO:1 and X03638 clearly identifies the paper by Noda as the source of the sequence, and indicates that the sequences are 74.2% identical, and contain local regions with as much as 86.2% identity. While claims 14 and 16 both recite "A purified human nucleic acid", the broadest reasonable interpretation of the claims includes any fragment or functional derivative thereof (see end of each claim), and the definition of functional derivatives in the

specification is so broad that it includes essentially any sequence, of any structure, and any function. Therefore the sequence from Noda anticipates claims 14 – 16. The reference by Noda also teaches that the nucleic acids are cloned into vectors (see for example p. 190, first column, which discusses vector sequences, and the text in the second column of p. 190, which refers to the clones by names such as prSCH109; note that the lowercase p is used to denote a plasmid vector). As Noda teaches the nucleic acids of claims 14-16 in vectors, the reference anticipates claims 17 – 19.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14 – 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noda (1986. Nature 320:188 – 192) in view of Wang (1997. J Clin Invest 99:1714-1720).

The reasons why claims 14 – 19 are anticipated by Noda are set forth in the rejection under 35 USC 102(b) above. Briefly, Noda teaches nucleic acids that are within the scope of claims 14 – 16, as well as vectors containing said nucleic acids. However Noda does not teach a cell harboring said vector, as recited in claims 20 – 22.

Wang teaches transfecting vectors comprising nucleic acids encoding sodium channels into cells, which is on point to claims 17 – 19 (vectors) and 20 – 22 (host cells; see p. 1715, Methods). Wang teaches that putting vectors comprising nucleic acids which encode sodium channels is useful for screening for drugs which for treating congenital long QT syndrome. Wang teaches that this disease is caused by mutations in the sodium channel SCN5A (see p.

17174, first column) and that drugs which inhibit sodium channels such as mexiletine and lidocaine are useful in treatment of arrhythmias (see p. 1714, second column, second complete paragraph). Furthermore Wang teaches assays to determine the degree to which various drugs such as mexiletine inhibit sodium channels (see for example p. 1716, Figure 2). However Wang does not teach the nucleic acid sequences of the invention, as recited in claims 14 – 16.

It would have been obvious to one of ordinary skill in the art to transfect the vectors from Noda into cells, as taught by Wang, thereby arriving at the invention of claims 20 – 22. The motivation to do so would be to screen for anti-arryhthmic drugs, and flows directly from the references themselves. Noda teaches nucleic acid sequences which encode sodium channels as well as vectors comprising same, and Wang teaches transfecting sodium-channel-encoding vectors into cells for screening for anti-arryhthmics, thereby guiding the artisan to put the vectors into cells.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Daniel E. Kolker, Ph.D.
August 17, 2006

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PRIMARY EXAMINER